Remarks/Arguments

The specification has been amended to correct the inadvertent typographical errors. With respect to the amendment made to page 25, SEQ ID NOS: 7 and 8 were replaced with SEQ ID NOS: 5 and 6, respectively, as the latter SEQ ID NOS: are the only two oligonucleotide primers set forth in the instant Sequence Listing. The incorrectly recited SEQ ID NOS: 7 and 8 are directed to the cDNA and the full-length amino acid sequence for the human long extracellular form of B7L-1, respectively. Since they cannot be used for the PCR cloning as described in Example 7, it must have been an inadvertent error. With respect to the amendment made to page 27, the term B7L-1 was replaced with LDCAM, where appropriate, to maintain the consistency that LDCAM is the antigen, as described in the first, non-amended paragraph of Example 10. The applicants thus believe that these amendments do not introduce any new matters.

Claims 18, 20, 22, 35-37, 46 and 55 have been amended, as suggested by the examiner, to limit the binding of the recited polypeptides to the binding target being LDCAM and B7L-1 with the specific SEQ ID NOS:. Claim 29 has been amended to limit the claimed polypeptide to comprise the extracellular domain, or a fragment thereof, which is soluble.

The applicants thank the examiner for providing the clarification to the statement made in paragraph No. 3 of the Office action of Paper No. 15.

Rejection under 35 U.S.C. § 112, second paragraph

The examiner maintains the rejection of claims 18-63 under 35 U.S.C. § 112, second paragraph, as being indefinite. The applicants request the rejection of claims 18-63 under same be withdrawn in view of the current amendment, which was made as suggested by the examiner. Regarding the rejection claims 35, 36 and 46-54 because of the language, "moderate stringency" and "severe stringency," reconsideration is respectfully requested. Applicants submit that the stringency conditions, as stated in the specification, are defined in Sambrook et al. (paragraph bridging pages 9 and 10). Furthermore, establishing a moderate or severe hybridization condition was known in the art at the time of filing. Applicants therefore submit that the claims are not indefinite because these terms are recited. Assuming *arguendo* that even if these conditions are not precise to the examiner, the applicants submit that the claims, according to *Hybritech Incorporated v. Monoclonal Antibodies, Inc.* (802 F.2d 1367, 231 USPQ 94, 95 (Fed. Cir. 1986)), be read in light of the specification, reasonably apprise those skilled in the art and are as precise as the subject matter permits. The applicants therefore respectfully request the examiner to withdraw this rejection.

Rejection under 35 U.S.C. § 112, first paragraph (non-enablement)

The examiner maintains the rejection of claims 18-63 under 35 U.S.C. § 112, first paragraph, alleging the same reasons as set forth in the Office action of Paper No. 15. In maintaining the rejection, the examiner reiterates that while the specification describes how to make the variant polypeptides and how to screen for the ones that are capable of binding to the target LDCAM and/or B7L1, it is not enabling because it does not teach "as to which residues should or should not be changed to preserve the recited function of binding to either a LDCAM or B7L-1 polypeptide." (Paper No. 21, page 3). To support this position, the examiner further re-cites Metzler et al., specifically Table 2 thereof, asserting that single amino acid changes can alter or abolish the ability of CTLA-4 to interact with CD80 and CD86.

The applicants respectfully disagree with the examiner on her characterization of Mertz et al., specifically the data presented in Table 2. Of the 9 mutations presented in Table 2, five of them exert little effect on binding to CD80 and four of them on the binding to CD86. In other words, not any amino acid changes would affect the protein binding, as alleged by the examiner, since about 50% of these single amino acid changes did not abolish the binding. This is not surprising because the data in Table 2 are presented to show that only the mutations that occur in the conserved surface patch on the A'GFCC' face abolish binding to CD80 and/or CD86, while the other mutations, which occur on the BED surface, did not (page 530, first col.). The data are not shown to demonstrate that any single amino acid changes would affect the binding activity of CTLA-4, as appeared to be implied by the examiner.

Regarding the examiner's rejection that is partly based on the binding target being "undefined," the applicants have amended to limit the binding target to LDCAM and/or B7L-1 with specific SEQ ID NOS:, thus effectively removing this part of the reason for the rejection.

The applicants thank the examiner for suggesting the claims being limited to "95%." However, the examiner fails to provide as to why a variant with this percentage identity is enabled but not are those with at least 80% or at least 90% of percentage identity.

The applicants wish to remind the examiner that the claims are drawn to an isolated polypeptide that is not only based on sequence identity or with a mutation, but also on its capability of binding to LDCAM and/or B7L-1. The disclosure provides : (1) the amino acid sequences, to which the claimed polypeptides are compared are provided (SEQ ID NOS: 2 and 4); (2) the structure of LDCAM, which is defined into extracellular, transmembrane, and cytoplasmic domains; and (3) suitable assays, which are used to determine the binding limitation. In view of this disclosure and that the level of the skilled in the art is high, the applicants submit that the full scope of the claims is enabled without undue experimentation.

In view of the foregoing discussion, the applicants respectfully request the examiner to withdraw this rejection.

Rejection under 35 U.S.C. § 102(e)

The examiner maintains the rejection, and makes new ground of rejection, of claims 18-63 as being anticipated by Baker et al. (US 2002/0198147), as evidenced by the alignments of record in Paper No. 15. Reconsideration of this rejection is respectfully requested. The examiner asserts that the applicants' Declaration under 37 CFR 1.131, filed May 27, 2003, is ineffective to overcome the rejection because "the reference is claiming the same patentable invention."

In maintaining and making the same rejection, the examiner asserts the following: (1) Baker et al. teach and claim (emphasis original) the isolated PRO355 polypeptide set forth in SEQ ID NO:61 (e.g., claim 12). (2) PRO355 differs from the instant SEQ ID NO:2 only by an internal deletion of two amino acids, at residues 24 and 25 of the latter. (3a) PRO355 differs from the instant SEQ ID NO:4 by an internal deletion of two amino acids, which correspond to residues 6 and 7 of SEQ ID NO:2, and by an additional amino acid at the C terminus. (3b) Despite of the amino acid difference as set forth in the preceding (3a), the examiner alleges that SEQ ID NO: 61 is 100% identical to SEQ ID NO: 2 and 4. (4) SEQ ID NO: 60 of Baker et al. would hybridize to the complement of the instant SEQ ID NOS: 1 and 3. (5) Baker et al. teach and claim methods of producing PRO355 by culturing a host cell transfected with SEQ ID NO:60. (6) Baker et al. teach and claim (emphasis original) fusion polypeptide comprising "the PRO355 polypeptide or a soluble extracellular domain (i.e., a fragment) thereof, including a fusion polypeptide comprising an Fc region. " (7) Variants of PRO355 polypeptide are also taught and claimed (emphasis original), citing paragraphs 180-187 and claims 12-13.

The applicants respectfully submit that the examiner has erred in concluding that Baker et al. anticipates the instant claims, hence the 102(e) rejection is not proper. The applicants further submit that Baker et al. does not claim all the subject matter that are instantly claimed by the applicants.

Baker et al. does not anticipate claims 18-63

Baker et al. does not anticipate the instant claims because the amino acid sequence of SEQ ID NO: 61 thereof is not the same as that in the instant SEQ ID NO: 2 or 4. SEQ ID NO: 61 is not the same as SEQ ID NO: 2 because the former is devoid of two amino acid residues that occur in the latter. SEQ ID NO: 61 is not the same as SEQ ID NO:4 because, when aligned to each other, the former differs from the latter in one amino acid, i.e., while residue 31 of SEQ ID NO:61 is Phenylalanine the aligned residue in SEQ ID NO: 4 is Leucine. Regarding the examiner's description of the amino acid difference between SEQ ID NO: 61 and SEQ ID NO: 4, the examiner is requested to clarify the description that SEQ ID NO: 61 differs from SEQ ID NO:4 by the two amino acid deletion and the additional amino acid in the C terminus; the applicants did not receive the comparison in the alignments of record in Paper No. 15. Because of the differences in the amino acid sequences, the applicants respectfully submit that the instantly claims are not anticipated by Baker et al. For a 102 reference to be anticipated, it must "disclose

each and every limitation of the claimed invention." *In re Paulsen*, 30 F.3d 1475, 1478 79, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994)

Baker et al. does not claim the same invention:

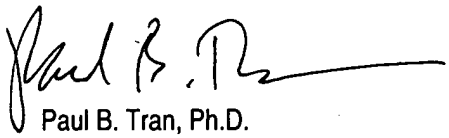
Assuming *arguendo* that, the amino acid difference as presented above notwithstanding, SEQ ID NO: 61 may be considered as identical to SEQ ID NO: 2 and 4, hence the 102(e) rejection is proper – which is not the case, contrary to the examiner's assertion that Baker et al. discloses and claims all the subject matter instantly claimed, the applicants respectfully submit that Baker et al. claims only the full-length PRO355, as do applicants in some of the claims. Baker et al. does not claim the following subject matter: the full-length polypeptide that is without the leader sequence; the extracellular domain, with or without the leader sequence; polypeptides that are soluble; fusion protein comprising soluble protein or extracellular domain; a composition comprising the polypeptide and a carrier. Furthermore, Baker neither discloses nor claims the oligomers comprising the polypeptide.

There are six claims drawn in Baker et al., claims 12-17. Except claim 14, which does not recite the ATCC deposit for PRO355, these claims are drawn to a polypeptide which is at least 80% identical or has a score of at least 80% positives to the full length SEQ ID NO: 61 or full length PRO355 protein, or to a chimeric molecule comprising any of these polypeptides. Nowhere in the claim set does Baker et al. recite a polypeptide which is as recited in the instant claims as summarized above. For this reason, the applicants respectfully request the examiner to reconsider the Declaration of May 27, 2003, and withdraw this rejection.

Conclusion

In view of the foregoing remarks, the applicants respectfully request that a timely Notice of Allowance be issued for this application.

Respectfully submitted,



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